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October 21, 2016

Versar, Inc.
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Delivered by email: perchlorate@versar.com

RE: PERCHLORATE PEER REVIEW

In response to the Federal Register Notice [81 FR 67347 (September 30, 2016)] and on behalf of the Perchlorate Study Group (PSG)[1], Intertox is pleased to submit comments regarding the interim list of peer reviewers. We appreciate that EPA has opted to hold two peer reviews, the first for the Biologically Based Dose Response (BBDR) model and the second to evaluate the implementation of the model results to derive a Maximum Contaminant Level Goal (MCLG). Given that this is the first time that EPA will develop a MCLG using BBDR modeling, the PSG is committed to assisting EPA, as the PSG has for over 15 years, to ensure that the information it disseminates adheres to the basic standards of quality, objectivity, utility, and integrity. It is in this spirit that Intertox provides comments on the interim list of peer reviewers.

Given the compressed time frame for public comment, we have not attempted to evaluate or recommend individual peer reviewers. Instead, we offer general observations that we hope will add value as you develop your process.

Comment 1

Standards of information quality, the assessment factors, and guidelines for peer reviewers would assist the peer reviewers in developing the most reliable assessment for the Agency. These are key documents for the peer review process and provide a level of transparency in the quality the Agency seeks.

- Guidelines for Ensuring and Maximizing the Quality, Objectivity, Utility, and Integrity of Information Disseminated by the Environmental Protection Agency (EPA Information Quality Guidelines).
- A Summary of General Assessment Factors for Evaluating the Quality of Scientific and Technical Information
- This 4th edition of the Peer Review Handbook was developed by the U.S. Environmental Protection Agency (hereafter EPA or the Agency) to provide guidance to EPA staff and managers who are planning and conducting peer reviews.

The Agency might want to add additional documents, but these will benefit the peer reviewers with the understanding of the need for quality of scientific information as well as what constitutes "quality" scientific information. In the meantime, how will EPA substantiate its approach as an evaluation of a solid standard scientific assessment per the IAQ guidance on influential information?

[1] *The Perchlorate Information Bureau is supported by Aerojet Rocketdyne, American Pacific Corporation, Lockheed Martin and Orbital-ATK. These companies have worked cooperatively with the U.S. Environmental Protection Agency to increase scientific and medical understanding of perchlorate's risk to human health.*

Comment 2

As stated in the FRN:

> Submit your comments on the interim list of peer review candidates and draft charge to Versar, Inc., no later than October 21,

And

> Questions concerning the interim list of expert peer review candidates and draft peer review charge questions should be directed to Versar, Inc.

The FRN states that this is an "interim list," but it is unclear the meaning of this term. Is it the intent of EPA or Versar to use the exact same peer reviewers for both peer review panels; will other peer reviewers be evaluated for the second panel; or will a subset be on both panels? Does EPA plan to look for additional experts to fill the subsequent peer review with another FRN?

Comment 3

Versar, Inc. assembled a panel of scientific experts to evaluate the draft BBDR model and draft report. EPA requests:[2]

> …scientific experts whom [sic] have knowledge and experience in one or more of the following areas: (1) Physiologically-based pharmacokinetic (PBPK), physiologically-based pharmacokinetic/pharmacodynamics (PBPK/PD) and/or Biologically Based Dose-Response (BBDR) modeling, (2) fetal and neonatal thyroid endocrinology (clinical and experimental), (3) iodide homeostasis, and (4) perchlorate toxicology and mode of action or adverse outcome pathway.

This is a limited set of four categories of expertise. On June 3, 2016, EPA sought to expand the expertise since it had combined two peer reviews into one peer review. Because of that, EPA requested additional experts in one or more of the following areas of risk assessment to include: [3]

> An understanding of thyroid function (preferably in the sensitive life stages of interest), the importance of maternal thyroid hormone homeostasis in each stage of gestation, hypothyroxinemia, neurodevelopmental assessment indices for young children including the Bayley's Scale, the toxicity of perchlorate, epidemiological assessment techniques, and statistics.

Clearly the expertise required for the first and second peer reviews are different. A number of the experts in the interim list of 19 peer reviewers appears to fulfill the requirements of the second, but not the first. Will Versar or EPA explain how each of the current group of interim experts fills the categories of expertise requested currently and in March?

Comment 4

The Agency's Peer Review Guidance (2015) states:

> It [Peer Review] is conducted by qualified individuals (or organizations) who are independent of those who performed the work and who are collectively equivalent in technical expertise to those who performed the original work (i.e., peers) [emphasis added].

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[2] Federal Register (81 FR 10617; March 1, 2016)
[3] Federal Register (81 FR 35760; June 3, 2016)

> Peer review is an in-depth assessment of the assumptions, calculations, extrapolations, alternate interpretations, methodology, acceptance criteria and conclusions pertaining to the scientific or technical work product, and of the documentation that supports them.

It is unclear what expertise was used to develop the model. If that information were made available, it would assist in obtaining the expertise necessary for this peer review. Additional expertise appears to be missing that would provide key insight to the evaluation of the BBDR model. How does the Agency envision that peer reviewers will assess the assumptions, calculations, extrapolations, *etc.* used by EPA, given the short time for the model review as well as the limitation on expertise? Additionally, to address possible issues of balance and quantity of work to be evaluated at least two, and preferably more, experts would fulfill each category. We suggest the interim list be expanded to include (but not be limited to) the following areas of expertise:

- Computer programming (two different platforms are offered; to evaluate the model codes); particularly experts in AcslX (Aegis Technologies) and R platforms (to provide guidance to experts on questions of software),
- Receptor pharmacology (to provide understanding of basic receptor ligand interactions relating to symporter function),
- Iodine regulation (clinical evaluations as well as iodine homeostasis, biochemistry, physiology, and lifecycle), and
- Statistical assessments (e.g., sensitivity analysis for BBDR models)
- Expert medical PBPK modelers (to compare the Agency's model with best available techniques and practice of modeling).

Comment 5

For this first peer review panel, it is unclear how the BBDR model code evaluation is expected to be conducted. Based on the biographies provided by the contractor, a number of candidates appear to have no experience with BBDR modeling. When they receive the model code, do Versar and EPA expect each panelist to download the model and run it prior to the public meetings? If not, why not? How does the Agency envision obtaining independent scientific advice regarding the model if the panelists cannot or do not run the model? How would EPA evaluate comments of a reviewer who has never run a model compared to a reviewer that has?

Thank you for the opportunity to provide these comments.

Sincerely,

Richard C. Pleus, PhD
Intertox, Inc.